10/509,732

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	("6380258").PN.	US-PGPUB; USPAT	OR	OFF	2007/07/01 20:42
L2	1	("7115632").PN.	US-PGPUB; USPAT	OR	OFF	2007/07/01 22:44
L3	389	(544/383,514/252.12,514/255.01). CCLS.	US-PGPUB; USPAT	OR	OFF	2007/07/01 22:52
L4	38	l3 and carbamic adj acid	US-PGPUB; USPAT	OR	ON	2007/07/01 22:53
L5	0	l4 and hdac	US-PGPUB; USPAT	OR	ON	2007/07/01 22:55
L6	37	l4 and (phenyl or aryl)	US-PGPUB; USPAT	OR	ON	2007/07/01 22:56
L7	32	l6 and carbonyl	US-PGPUB; USPAT	OR	ON	2007/07/01 22:58
L8	27	l7 and sulfonyl	US-PGPUB; USPAT	OR	ON	2007/07/01 22:58

10/509,732 search after election

10/513699

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PASSWORD:
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NEWS  1          Web Page for STN Seminar Schedule - N. America
NEWS  2  MAR 15  WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS  3  MAR 16  CASREACT coverage extended
NEWS  4  MAR 20  MARPAT now updated daily
NEWS  5  MAR 22  LWPI reloaded
NEWS  6  MAR 30  RDISCLOSURE reloaded with enhancements
NEWS  7  APR 02  JICST-EPLUS removed from database clusters and STN
NEWS  8  APR 30  GENBANK reloaded and enhanced with Genome Project ID field
NEWS  9  APR 30  CHEMCATS enhanced with 1.2 million new records
NEWS 10  APR 30  CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS 11  APR 30  INPADOC replaced by INPADOCDB on STN
NEWS 12  MAY 01  New CAS web site launched
NEWS 13  MAY 08  CA/CAplus Indian patent publication number format defined
NEWS 14  MAY 14  RDISCLOSURE on STN Easy enhanced with new search and display
                 fields
NEWS 15  MAY 21  BIOSIS reloaded and enhanced with archival data
NEWS 16  MAY 21  TOXCENTER enhanced with BIOSIS reload
NEWS 17  MAY 21  CA/CAplus enhanced with additional kind codes for German
                 patents
NEWS 18  MAY 22  CA/CAplus enhanced with IPC reclassification in Japanese
                 patents
NEWS 19  JUN 27  CA/CAplus enhanced with pre-1967 CAS Registry Numbers
NEWS 20  JUN 29  STN Viewer now available
NEWS 21  JUN 29  STN Express, Version 8.2, now available

NEWS EXPRESS  29 JUNE 2007:  CURRENT WINDOWS VERSION IS V8.2,
              CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
              AND CURRENT DISCOVER FILE IS DATED 4 MAY 2007.

NEWS HOURS    STN Operating Hours Plus Help Desk Availability
NEWS LOGIN    Welcome Banner and News Items
NEWS IPC8     For general information regarding STN implementation of IPC 8
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Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * *

<12/04/2007> Erich Leese

10/513699

FILE 'HOME' ENTERED AT 20:54:27 ON 01 JUL 2007

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=> file reg
COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                               ENTRY     SESSION
FULL ESTIMATED COST                             0.21        0.21
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FILE 'REGISTRY' ENTERED AT 20:54:38 ON 01 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 JUN 2007 HIGHEST RN 940349-93-9
DICTIONARY FILE UPDATES: 29 JUN 2007 HIGHEST RN 940349-93-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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=>
Uploading C:\Program Files\Stnexp\Queries\10509732withQ1.str

L1      STRUCTURE UPLOADED

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SAMPLE SEARCH INITIATED 20:54:56 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      394 TO ITERATE

100.0% PROCESSED      394 ITERATIONS                          5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          6690 TO      9070
PROJECTED ANSWERS:                5 TO       234

L2            5 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 20:54:59 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      7671 TO ITERATE

100.0% PROCESSED     7671 ITERATIONS                         82 ANSWERS
SEARCH TIME: 00.00.01
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10/513699

L3 82 SEA SSS FUL L1

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COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                               ENTRY     SESSION
FULL ESTIMATED COST                            172.10      172.31
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FILE 'CAPLUS' ENTERED AT 20:55:05 ON 01 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 1 Jul 2007 VOL 147 ISS 2
FILE LAST UPDATED: 29 Jun 2007 (20070629/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

```
=> s l3 full
L4            25 L3

=> d ibib abs hitstr tot

L4   ANSWER 1 OF 25  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:441608  CAPLUS
TITLE:                    A quantitative structure-activity relationship study
                          on matrix metalloproteinase inhibitors: piperidine
                          sulfonamide aryl hydroxamic acid analogs
AUTHOR(S):                Kumaran, S.; Gupta, S. P.
CORPORATE SOURCE:         Department of Pharmacy, Birla Institute of Technology
                          and Science, Pilani, 333031, India
SOURCE:                   Journal of Enzyme Inhibition and Medicinal Chemistry
                          (2007), 22(1), 23-27
                          CODEN: JEIMAZ; ISSN: 1475-6366
PUBLISHER:                Informa Healthcare
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
```

AB A quant. structure-activity relationship (QSAR) study has been made on a series of piperidine sulfonamide aryl hydroxamic acid analogs acting as matrix metalloproteinase (MMP) inhibitors. The inhibitory potencies of the compds. against two MMPs, MMP-2 and MMP-13, are found to be significantly correlated with the hydrophobic properties of the mols., suggesting that in both enzymes the hydrophobic interaction is playing a dominant role.

```
IT   308385-85-5
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
```

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10/513699

(Biological study); PRP (Properties)
(QSAR study on inhibitors of matrix metalloproteinases 2 and 13)

```
RN   308385-85-5  CAPLUS
CN   Benzamide, 2-[(4-benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy-  (9CI)  (CA
     INDEX NAME)
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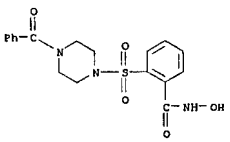

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REFERENCE COUNT:          24    THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4   ANSWER 2 OF 25  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:216815  CAPLUS
DOCUMENT NUMBER:          146:434176
TITLE:                    Novel Selective Inhibitors of the Zinc Plasmodial
                          Aminopeptidase PfA-M1 as Potential Antimalarial Agents
AUTHOR(S):                Flipo, Marion; Beghyn, Terence; Leroux, Virginie;
                          Florent, Isabelle; Deprez, Benoit P.; Deprez-Poulain,
                          Rebecca F.
CORPORATE SOURCE:         Biostructures and Drug Discovery, Inserm U761, Lille,
                          F-59006, Fr.
SOURCE:                   Journal of Medicinal Chemistry (2007), 50(6),
                          1322-1334
                          CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER:                American Chemical Society
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
GI
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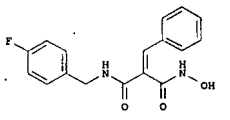

AB Proteases that are expressed during the erythrocytic stage of Plasmodium falciparum are newly explored drug targets for the treatment of malaria. The authors report here the discovery of potent inhibitors of PfA-M1, a metallo-aminopeptidase of the parasite. These compds. are based on a malonic hydroxamic template and present a very good selectivity toward neutral aminopeptidase (APN-CD13), a related protease in mammals. Structure-activity relationships in these series are described. Further

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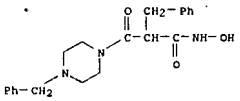
optimization of the best inhibitor yielded a nanomolar, selective inhibitor of PfA-M1 (I). This inhibitor displays good physicochem. and pharmacokinetic properties and a promising antimalarial activity.

IT 934618-87-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(selective inhibitors of zinc plasmodial aminopeptidase PfA-M1 as potential antimalarial agents)

RN 934618-87-8 CAPLUS
CN 1-Piperazinepropanamide, N-hydroxy-β-oxo-α,4-bis(phenylmethyl)- (CA INDEX NAME)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1245530 CAPLUS
DOCUMENT NUMBER: 146:155298
TITLE: A library of novel hydroxamic acids targeting the metallo-protease family: Design, parallel synthesis and screening
AUTHOR(S): Flipo, Marion; Beghyn, Terence; Charton, Julie; Leroux, Virginie A.; Deprez, Benoit P.; Deprez-Poulain, Rebecca F.
CORPORATE SOURCE: Inserm, U761, Faculty of Pharmacy, Inst. Pasteur Lille, Lille, F-59006, Fr.
SOURCE: Bioorganic & Medicinal Chemistry (2007), 15(1), 63-76
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors report here the design and parallel synthesis of 217 compds. based on a malonic-hydroxamic acid template. These compds. are obtained via a two-step solution-phase procedure. The set of diverse building-blocks used makes this strategy suitable for the search of inhibitors of various metallo-proteases and for the investigation of the biol. role of new metallo-proteases. As a proof of concept, the authors screened this library on neutral aminopeptidase (APN; E.C. 3.4.11.2), the prototypal enzyme of the M1 family. Several submicromolar inhibitors were identified.

IT 260438-45-7P 919996-11-5P 919996-12-6P
919996-19-3P 919996-95-5P 919997-02-7P
919997-21-0P 919997-22-1P 919997-29-8P
919997-57-2P 919997-58-3P 919997-65-2P
919997-97-0P 919997-99-2P 919998-10-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(design, parallel synthesis and screening of hydroxamic acids targeting the metallo-protease)

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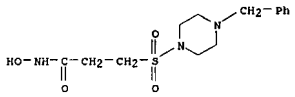

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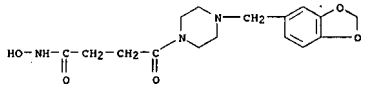

RN 919996-12-6 CAPLUS
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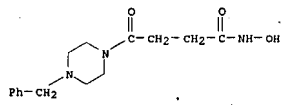
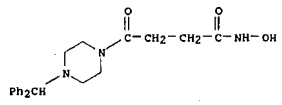
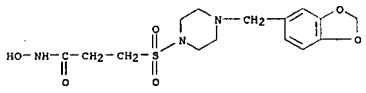


RN 919996-19-3 CAPLUS
CN 1-Piperazinebutanamide, 4-(diphenylmethyl)-N-hydroxy- γ-oxo- (CA INDEX NAME)



RN 919996-95-5 CAPLUS
CN Propanamide, 3-[[4-(1,3-benzodioxol-5-ylmethyl)-1-piperazinyl]sulfonyl]-N-

hydroxy- (CA INDEX NAME)



RN 919997-02-7 CAPLUS
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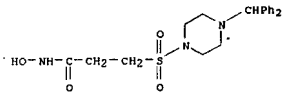

RN 919997-21-0 CAPLUS
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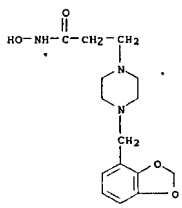

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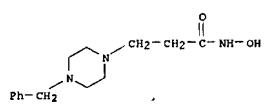
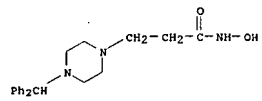
CN 1-Piperazinepropanamide, N-hydroxy-4-(phenylmethyl)- (CA INDEX NAME)



RN 919997-29-8 CAPLUS
CN 1-Piperazinepropanamide, 4-(diphenylmethyl)-N-hydroxy- (CA INDEX NAME)



RN 919997-57-2 CAPLUS
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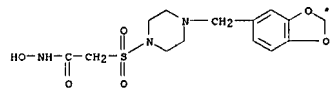

RN 919997-58-3 CAPLUS
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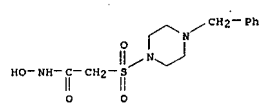

RN 919997-65-2 CAPLUS
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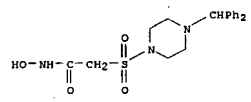

RN 919997-97-0 CAPLUS
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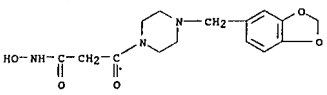

RN 919997-99-2 CAPLUS
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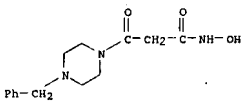

RN 919998-10-0 CAPLUS
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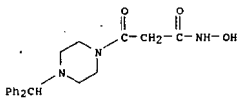

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1024194 CAPLUS
DOCUMENT NUMBER: 145:397368
TITLE: Preparation of sulfonyl aryl or heteroaryl hydroxamic acid compounds as matrix metalloprotease inhibitors
INVENTOR(S): Bedell, Louis J.; Mcdonald, Joseph J.; Barta, Thomas E.; Becker, Daniel P.; Shashidhar, Rao N.; Freskos, John N.; Mischke, Brent V.; Getman, Daniel P.; Decrescenzo, Gary A.; Villamil, Clara I.
PATENT ASSIGNEE(S): G. D. Searle & Co., USA
SOURCE: U.S., 162pp., Cont.-in-part of U.S. Ser. No. 310,813.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 7115632	B1	20061003	US 2000-569034	20000511

US 2001020021	A1	20010906	US 1999-230209	19990624
US 6380258	B2	20020430		
WO 2001085680	A2	20011115	WO 2001-US14706	20010507
WO 2001085680	A3	20020307		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2003073845	A1	20030417	US 2001-909227	20010719
US 6696449	B2	20040224		

PRIORITY APPLN. INFO.:

US 1999-310813	B2	19990512
US 1999-230209	A2	19990624
US 1997-35182P	P	19970304
WO 1998-US4300	W	19980304
US 2000-569034	A	20000511
US 2000-728408	A2	20001201

OTHER SOURCE(S): MARPAT 145:397368
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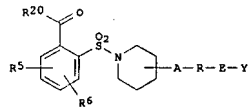


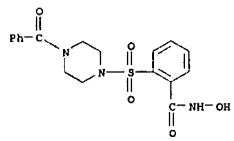
I

AB The title compds. [I; A = O, S, CO2, etc.; R = alkyl, alkoxyalkyl, aryl, etc.; E = CO, SO2, (un)substituted CONH, etc.; Y = H, alkyl, alkoxy, etc.; R5, R6 = H, alkyl, cycloalkyl, etc.; R20 = OR21, NR13OR22, etc. (R13 = H, alkyl, benzyl; R21 = alkyl, aryl, arylalkyl; R22 = selectively removable protecting group)] or pharmaceutically acceptable salts thereof that inter alia inhibit matrix metalloprotease activity, are prepared Thus, thioetherification of 4-phenoxybenzenethiol with 2-fluorobenzaldehyde in the presence of K2CO3 in isopropanol under reflux for 20 h gave 2-(4-phenoxyphenylthio)benzaldehyde which was condensed with tetra-Et dimethylaminomethylenediphosphonate in the presence of NaH in THF at room temperature for 4 h gave to 2-[2-(4-phenoxyphenylthio)phenyl]acetic acid (II). II was oxidized by H2O2 in acetic acid to 2-[2-(4-phenoxyphenylsulfonyl)phenyl]acetic acid which was condensed with O-tetrahydropyranylhydroxylamine using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in MeCN followed by treatment with p-toluenesulfonic acid in methanol at room temperature for 2 h to give N-hydroxy-2-[2-(4-phenoxyphenylsulfonyl)phenyl]acetamide (III). III and N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide showed IC50 of >10,000 nM against MMP-1, 0.3 and 2.4 nM, resp., against MMP-2, and 2 and 2.7 nM, resp., against

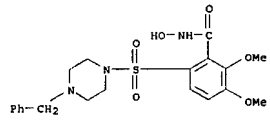
MMP-13. Also disclosed is a treatment process that comprises administering a contemplated sulfonyl aromatic or heteroarom. ring hydroxamic acid compound in a matrix metalloprotease (MMP) enzyme-inhibiting effective amount to a host having a condition associated with pathol. MMP activity.

IT 308385-85-5P 308385-86-6P 308385-87-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonyl aryl or heteroaryl hydroxamic acid compds. as matrix metalloprotease inhibitors)

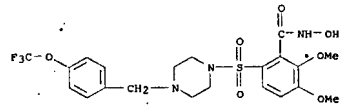
RN 308385-85-5 CAPLUS
CN Benzamide, 2-[(4-benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 308385-86-6 CAPLUS
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 308385-87-7 CAPLUS
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-[[4-(trifluoromethoxy)phenyl]methyl]-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:101557 CAPLUS
DOCUMENT NUMBER: 144:171021
TITLE: Preparation of piperazine and related N-hydroxy succinic acid diamide derivatives as metalloproteinase inhibitors with therapeutic uses
INVENTOR(S): Swinnen, Dominique; Bombrun, Agnes; Gonzalez, Jerome; Crosignani, Stefano; Gerber, Patrick; Jorand-Lebrun, Catherine
PATENT ASSIGNEE(S): Applied Research Systems Ars Holding N.V., Neth. Antilles
SOURCE: PCT Int. Appl., 203 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006010751	A1	20060202	WO 2005-EP53616	20050725

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2005266313	A1	20060202	AU 2005-266313	20050725
CA 2570903	A1	20060202	CA 2005-2570903	20050725
EP 1771421	A1	20070411	EP 2005-772035	20050725

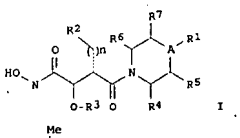
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU

CN 1989106	A	20070627	CN 2005-80025086	20050725
IN 2006DN07460	A	20070622	IN 2006-DN7460	20061211
NO 2007000994	A	20070426	NO 2007-994	20070221

PRIORITY APPLN. INFO.:

EP 2004-103574	A	20040726
US 2004-591111P	P	20040726
EP 2005-100641	A	20050131
US 2005-648924P	P	20050201
WO 2005-EP53616	W	20050725

OTHER SOURCE(S): MARPAT 144:171021
GI



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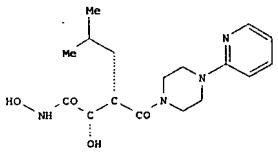


II

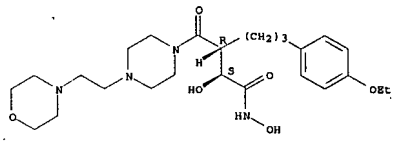
AB The present invention is related to piperazine and related N-hydroxy succinic acid diamide derivs. (shown as I; variables defined below; e.g. (2S,3S)-N-hydroxy-2-hydroxy-5-methyl-3-[[4-(2-pyridinyl)-1-piperazinyl]carbonyl]hexanamide (shown as II)) and use thereof, in particular for the treatment and/or prophylaxis of autoimmune disorders, inflammatory diseases, cardiovascular diseases, neurodegenerative diseases, cancer, respiratory diseases and fibrosis, including multiple sclerosis, arthritis, emphysema, chronic obstructive pulmonary disease, liver and pulmonary fibrosis. A = -C(B)- and N; B is H or B forms a bond with either R5 or R7; R1 = H, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, C3-C8-cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C3-C8-cycloalkyl C1-C6 alkyl, heterocycloalkyl C1-C6 alkyl, heteroaryl C1-C6 alkyl, amino and alkoxy; R2 = H, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, C3-C8-cycloalkyl, heterocycloalkyl, alkoxy, aryl and heteroaryl; R3 = H, C1-C6 alkyl, C2-C6 alkenyl and C2-C6 alkynyl; R4, R5, R6 and R7 = H, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl; or R4 and R7 form together a -CH2- linkage; n is an integer = 1, 2, 3, 4, 5 and 6; Carbons (2) and (3) are two chiral centers, wherein chiral center (2) has a configuration = S and R and wherein chiral center (3) has a S configuration as well as pharmaceutically acceptable salts thereof. Methods of preparation are claimed and prepns. and/or characterization data for .apprx.90 examples of I are included. For example, II was prepared from a 55/45 mixture of (2S)- and (2R)-pentafluorophenyl 2-((4S)-2,2-dimethyl-5-oxo-1,3-dioxolan-4-yl)-4-methylpentanoate (preparation by partial diastereoisomerization of latter isomer) by 1st creating an amide linkage using 1-(2-pyridyl)piperazine (40 %) and then a 2nd amide linkage using hydroxylamine (31 %). IC50 values for inhibition of MMP-1, MMP-2, MMP-9 and MMP-12 by 16 examples of I are tabulated. Also, percentage of inhibition of IL-2-induced peritoneal recruitment of lymphocytes (model for cellular migration that occurs during inflammation) by 8 examples of I are tabulated.

IT 874646-99-8P, (2S,3R)-6-(4-Ethoxyphenyl)-N-hydroxy-2-hydroxy-3-[[4-[2-(morpholin-4-yl)ethyl]piperazin-1-yl]carbonyl]hexanamide
874647-38-8P, (2S,3R)-6-(4-Ethoxyphenyl)-N-hydroxy-2-hydroxy-3-[[4-[2-(2-thienyl)ethyl]piperazin-1-yl]carbonyl]hexanamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of piperazine and related N-hydroxy succinic acid diamide deriv. as metalloproteinase inhibitors with therapeutic uses)

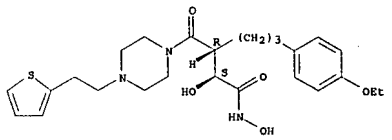
RN 874646-99-8 CAPLUS
CN 1-Piperazinebutanamide, β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-4-[2-(4-morpholinyl)ethyl]- γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 874647-38-8 CAPLUS
CN 1-Piperazinebutanamide, β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-γ-oxo-4-[2-(2-thienyl)ethyl]-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



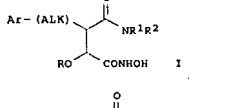
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:182646 CAPLUS
DOCUMENT NUMBER: 142:280227
TITLE: Preparation of hydroxamates as matrix metalloproteinase inhibitors
INVENTOR(S): Pain, Gilles; Davies, Stephen John; Bombrun, Agnes
PATENT ASSIGNEE(S): Vernalis Oxford Limited, UK; Laboratoires Serono S.A.
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

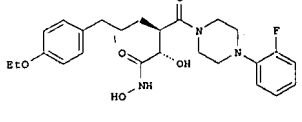
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2005019194	A1	20050303	WO 2004-GB3558		20040818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004266896	A1	20050303	AU 2004-266896		20040818
CA 2536576	A1	20050303	CA 2004-2536576		20040818
EP 1660471	A1	20060531	EP 2004-768117		20040818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
JP 2007503422	T	20070222	JP 2006-524410		20040818
CN 1930139	A	20070314	CN 2004-80023748		20040818
NO 2006001302	A	20060519	NO 2006-1302		20060322
IN 2006CN00997	A	20070615	IN 2006-CN997		20060323
US 2006281920	A1	20061214	US 2006-568433		20060808
PRIORITY APPLN. INFO.:			GB 2003-19917	A	20030823
			GB 2003-28632	A	20031210
			WO 2004-GB3558	W	20040818

OTHER SOURCE(S): CASREACT 142:280227; MARPAT 142:280227
GI



I



II

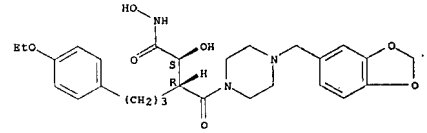
AB Title compds. I [wherein Ar = (un)substituted (hetero)aryl or (hetero)cycloalkyl; R = H or (cyclo)alkyl; Alk = alkylene or alkenylene; R1 and R2 link together to form (un)substituted heterocycloalkyl rings which is optionally fused to (un)substituted (hetero)cycloalkyl rings; and enantiomers, diastereoisomers, salts, hydrates or solvates thereof] were prepared as inhibitors of matrix metalloproteinases. For example, II was synthesized starting from (2S)-Hydroxysuccinic acid diisopropyl ester in several steps, which showed inhibitory activity against MMP-9, MMP-2, MMP-1 and MMP-12 with IC50 values of <100 nM, <100 nM, >10000 nM, <100 nM, resp. II also showed 57% inhibition of IL2-induced peritoneal recruitment

of lymphocytes at the dose of 3 mg/kg (vs. 76% inhibition by dexamethasone at the dose of 1 mg/kg). In general, I are selective inhibitors of MMP-12 and MMP-9 relative to the collagenases and stromelysins. Therefore, I and pharmaceutical compns. thereof are useful in the treatment or prophylaxis of diseases or conditions primarily mediated by MMP-12 and/or MMP-9, especially inflammatory conditions, such as multiple sclerosis and fibrosis.

IT 847037-92-7P, (3R)-[[4-[(Benzodioxol-5-yl)methyl]piperazin-1-yl]carbonyl]-6-(4-ethoxyphenyl)-(2S)-hydroxyhexanoic acid hydroxyamide
847037-94-9P, 6-(4-Ethoxyphenyl)-(2S)-hydroxy-(3R)-[[4-[(pyridin-4-yl)methyl]piperazin-1-yl]carbonyl]hexanoic acid hydroxyamide
847037-96-1P, 6-(4-Ethoxyphenyl)-(2S)-hydroxy-(3R)-[[4-benzylpiperazin-1-yl)carbonyl]hexanoic acid hydroxyamide
847038-26-0P, 4-[4-[(Benzodioxol-5-yl)methyl]piperazin-1-yl]-(2S)-hydroxy-N-hydroxy-4-oxo-(3R)-(4-trifluoromethoxybenzyl)butyramide
847038-34-0P, 4-[4-[(Benzodioxol-5-yl)methyl]piperazin-1-yl]-(3R)-(4-benzyloxybenzyl)-(2S)-hydroxy-N-hydroxy-4-oxobutyramide
847038-48-6P, 6-(4-Ethoxyphenyl)-(2S)-hydroxy-(3R)-[[4-[(4-trifluoromethoxyphenyl)sulfonyl]piperazin-1-yl]carbonyl]hexanoic acid hydroxyamide 847038-50-0P, 6-(4-Ethoxyphenyl)-(2S)-hydroxy-(3R)-[[4-(4-tolylsulfonyl)piperazin-1-yl]carbonyl]hexanoic acid hydroxyamide
847038-52-2P, (3R)-[[4-[(5-Bromothien-2-yl)sulfonyl]piperazin-1-yl]carbonyl]-6-(4-ethoxyphenyl)-(2S)-hydroxyhexanoic acid hydroxyamide
847038-54-4P, (3R)-[[4-[(5-Phenylsulfonylthien-2-yl)sulfonyl]piperazin-1-yl]carbonyl]-6-(4-ethoxyphenyl)-(2S)-hydroxyhexanoic acid hydroxyamide 847038-56-6P, (3R)-[[4-(4-Butoxyphenylsulfonyl)piperazin-1-yl]carbonyl]-6-(4-ethoxyphenyl)-(2S)-hydroxyhexanoic acid hydroxyamide 847038-58-8P, 6-(4-Ethoxyphenyl)-(2S)-hydroxy-(3R)-[[4-(4-methoxy-2,3,6-trimethylphenylsulfonyl)piperazin-1-yl]carbonyl]hexanoic acid hydroxyamide
847038-60-2P, (3R)-[[4-[(3,4-Dimethoxyphenyl)sulfonyl]piperazin-1-yl]carbonyl]-6-(4-ethoxyphenyl)-(2S)-hydroxyhexanoic acid hydroxyamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitor; preparation of hydroxamates as MMP inhibitors)

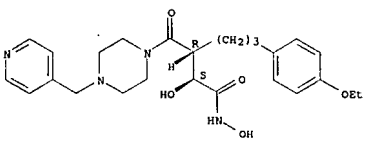
RN 847037-92-7 CAPLUS
CN 1-Piperazinebutanamide, 4-(1,3-benzodioxol-5-ylmethyl)- β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



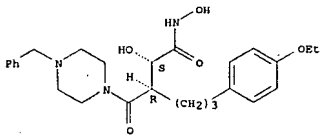
RN 847037-94-9 CAPLUS
CN 1-Piperazinebutanamide, β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-γ-oxo-4-(4-pyridinylmethyl)-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



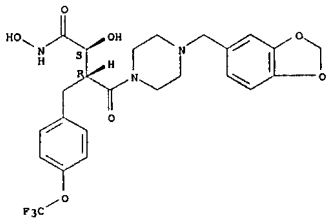
RN 847037-96-1 CAPLUS
CN 1-Piperazinebutanamide, β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-γ-oxo-4-(phenylmethyl)-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 847038-26-0 CAPLUS
CN 1-Piperazinebutanamide, 4-(1,3-benzodioxol-5-ylmethyl)-N, α-dihydroxy-γ-oxo-β-[[4-(trifluoromethoxy)phenyl]methyl]-, (αS,βR)- (9CI) (CA INDEX NAME)

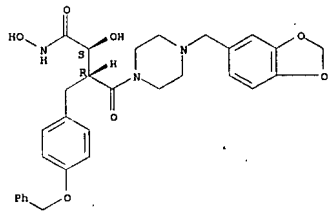
Absolute stereochemistry.



RN 847038-34-0 CAPLUS

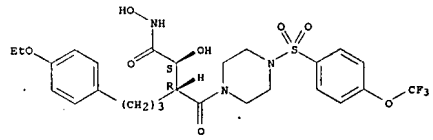
CN 1-Piperazinebutanamide, 4-(1,3-benzodioxol-5-ylmethyl)-N, α-dihydroxy-γ-oxo-β-[[4-(phenylmethoxy)phenyl]methyl]-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



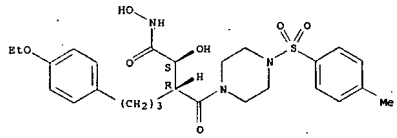
RN 847038-48-6 CAPLUS
CN 1-Piperazinebutanamide, β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-γ-oxo-4-[[4-(trifluoromethoxy)phenyl]sulfonyl]-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



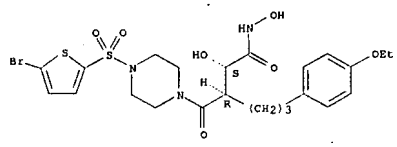
RN 847038-50-0 CAPLUS
CN 1-Piperazinebutanamide, β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-4-[(4-methylphenyl)sulfonyl]- γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



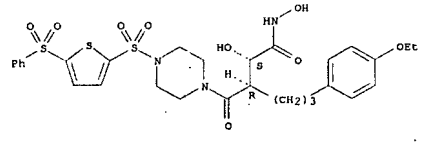
RN 847038-52-2 CAPLUS
CN 1-Piperazinebutanamide, 4-[(5-bromo-2-thienyl)sulfonyl]- β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



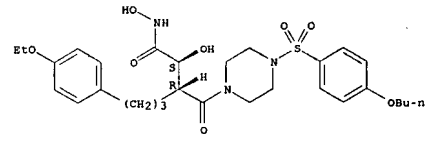
RN 847038-54-4 CAPLUS
CN 1-Piperazinebutanamide, β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-γ-oxo-4-[[5-(phenylsulfonyl)-2-thienyl]sulfonyl]-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



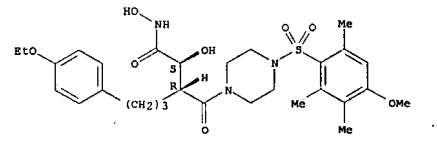
RN 847038-56-6 CAPLUS
CN 1-Piperazinebutanamide, 4-[(4-butoxyphenyl)sulfonyl]- β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



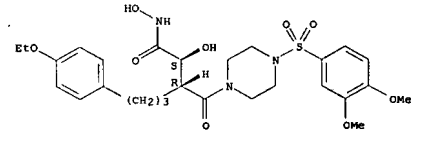
RN 847038-58-8 CAPLUS
CN 1-Piperazinebutanamide, β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-4-[(4-methoxy-2,3,6-trimethylphenyl)sulfonyl]- γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 847038-60-2 CAPLUS
CN 1-Piperazinebutanamide, 4-[(3,4-dimethoxyphenyl)sulfonyl]- β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:796490 CAPLUS
DOCUMENT NUMBER: 139:307794
TITLE: Preparation of N-hydroxy (piperazinesulfonyl)- or (piperazinecarbonyl)arylpropenamides as inhibitors of histone deacetylase and antiproliferative agents for

In Start Case

the treatment of cancer and psoriasis

INVENTOR(S): Watkins, Clare J.; Romero-Martin, Maria-Rosario; Ritchie, James; Finn, Paul W.; Kalvinsh, Ivars; Loza, Einars; Dikovska, Klara; Starchenkov, Igor; Lolya, Daina; Gailite, Vija

PATENT ASSIGNEE(S): Prolifix Limited, UK

SOURCE: PCT Int. Appl., 217 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082288	A1	20031009	WO 2003-GB1463	20030403
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2479906	A1	20031009	CA 2003-2479906	20030403
AU 2003229883	A1	20031013	AU 2003-229883	20030403
BR 2003008908	A	20050104	BR 2003-8908	20030403
EP 1492534	A1	20050105	EP 2003-722719	20030403
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005143385	A1	20050630	US 2003-509732	20030403
JP 2005527556	T	20050915	JP 2003-579825	20030403
NZ 536116	A	20070126	NZ 2003-536116	20030403
NO 2004004744	A	20041102	NO 2004-4744	20041102

PRIORITY APPLN. INFO.: US 2002-369337P P 20020403
WO 2003-GB1463 W 20030403

OTHER SOURCE(S): MARPAT 139:307794

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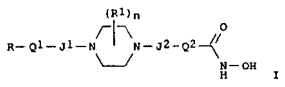

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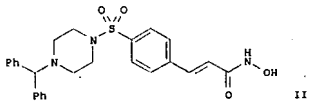
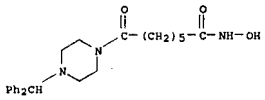


II

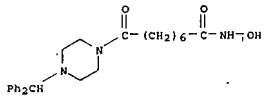
AB N-hydroxyamides I [J1 = single bond, C(:O), J2 = C(:O), SO2; Q1 = single bond, OX, SX, XOY, XSY, XO, XS; Q2 = (un)substituted C4-C8 alkylene at least four carbon atoms in length; R = (un)substituted cycloalkyl, heterocycloalkyl, or aryl; R1 = C1-C4 alkyl; X, Y = (un)substituted alkanediyl; n = 0-8] containing piperazine moieties, particularly N-hydroxy piperazinesulfonylarylpropenamides such as II, are prepared as inhibitors of histone deacetylase (HDAC) for the treatment of proliferative diseases, cancer, and psoriasis in both humans and animals. Biol. data on the inhibition of HDAC in vitro, the inhibition of cellular proliferation in vitro, and the in vivo testing of I on mice containing i.p. P388 tumors are given for a subset of I. Most of the compds. I tested inhibit HDAC with IC50 values between 20 nM and 200 nM, inhibit proliferation of four cell lines with IC50 values between 1 μM and 10 μM, and give log rank statistics for mice with P388 tumors (5 each) of between -3 and -5. II gives a log rank statistic for tumors in five mice of -9.62. Preparative data for approx. fifty of the title compds. are given.

IT 610801-00-8P 610801-02-0P 610801-14-4P
610801-15-5P 610801-16-6P 610801-17-7P
610801-21-3P 610801-40-6P 610801-42-8P
610801-43-9P 610801-44-0P 610801-46-2P
610801-50-8P 610801-51-9P 610801-57-5P
610801-58-6P 610801-63-3P 610801-70-2P
610801-71-3P 610801-72-4P 610801-73-5P
610801-76-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compds.; preparation of N-hydroxy (piperazinesulfonyl)- or (piperazinecarbonyl)arylpropenamides as inhibitors of histone deacetylase and antiproliferative agents for the treatment of cancer and psoriasis)

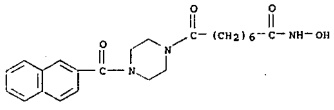
RN 610801-00-8 CAPLUS
CN 1-Piperazineheptanamide, 4-(diphenylmethyl)-N-hydroxy-ζ-oxo- (9CI). (CA INDEX NAME)



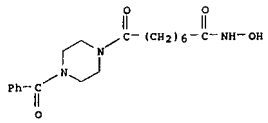
RN 610801-02-0 CAPLUS
CN 1-Piperazineoctanamide, 4-(diphenylmethyl)-N-hydroxy-η-oxo- (9CI) (CA INDEX NAME)



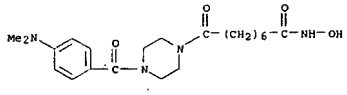
RN 610801-14-4 CAPLUS
CN 1-Piperazineoctanamide, N-hydroxy-4-(2-naphthalenylcarbonyl)-η-oxo- (9CI) (CA INDEX NAME)



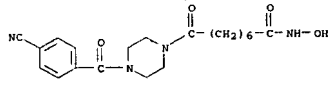
RN 610801-15-5 CAPLUS
CN 1-Piperazineoctanamide, 4-benzoyl-N-hydroxy-η-oxo- (9CI) (CA INDEX NAME)



RN 610801-16-6 CAPLUS
CN 1-Piperazineoctanamide, 4-[4-(dimethylamino)benzoyl]-N-hydroxy-η-oxo- (9CI) (CA INDEX NAME)

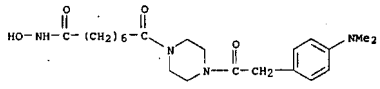


RN 610801-17-7 CAPLUS
CN 1-Piperazineoctanamide, 4-(4-cyanobenzoyl)-N-hydroxy-η-oxo- (9CI) (CA INDEX NAME)

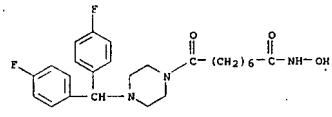


RN 610801-21-3 CAPLUS
CN 1-Piperazineoctanamide, 4-[[4-(dimethylamino)phenyl]acetyl]-N-hydroxy-

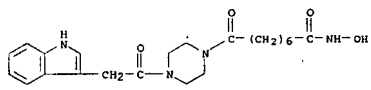
η-oxo- (9CI) (CA INDEX NAME)



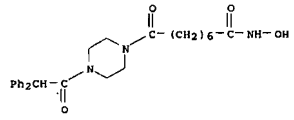
RN 610801-40-6 CAPLUS
CN 1-Piperazineoctanamide, 4-[bis(4-fluorophenyl)methyl]-N-hydroxy-η-oxo- (9CI) (CA INDEX NAME)



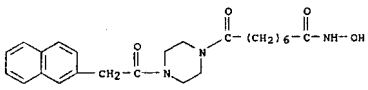
RN 610801-42-8 CAPLUS
CN 1-Piperazineoctanamide, N-hydroxy-4-(1H-indol-3-ylacetyl)-η-oxo- (9CI) (CA INDEX NAME)



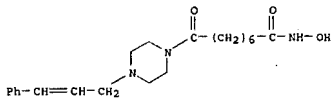
RN 610801-43-9 CAPLUS
CN 1-Piperazineoctanamide, 4-(diphenylacetyl)-N-hydroxy-η-oxo- (9CI) (CA INDEX NAME)



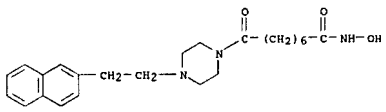
RN 610801-44-0 CAPLUS
CN 1-Piperazineoctanamide, N-hydroxy-4-(2-naphthalenylacetyl)-η-oxo- (9CI) (CA INDEX NAME)



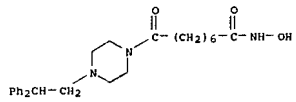
RN 610801-46-2 CAPLUS
CN 1-Piperazineoctanamide, N-hydroxy-η-oxo-4-(3-phenyl-2-propenyl)- (9CI) (CA INDEX NAME)



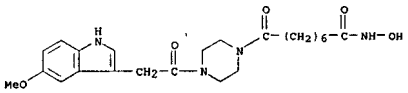
RN 610801-50-8 CAPLUS
CN 1-Piperazineoctanamide, N-hydroxy-4-[2-(2-naphthalenyl)ethyl]- η-oxo- (9CI) (CA INDEX NAME)



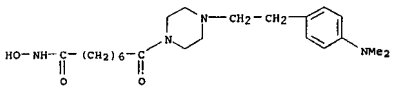
RN 610801-51-9 CAPLUS
CN 1-Piperazineoctanamide, 4-(2,2-diphenylethyl)-N-hydroxy- η-oxo- (9CI) (CA INDEX NAME)



RN 610801-57-5 CAPLUS
CN 1-Piperazineoctanamide, N-hydroxy-4-[(5-methoxy-1H-indol-3-yl)acetyl]- η-oxo- (9CI) (CA INDEX NAME)



RN 610801-58-6 CAPLUS
CN 1-Piperazineoctanamide, 4-[2-[4-(dimethylamino)phenyl]ethyl]-N-hydroxy-η-oxo- (9CI) (CA INDEX NAME)



RN 610801-63-3 CAPLUS
CN 1-Piperazineoctanamide, N-hydroxy-4-[2-(5-methoxy-1H-indol-3-yl)ethyl]-η-oxo-, ethanedioate (10:13) (salt) (9CI) (CA INDEX NAME)

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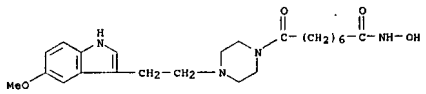
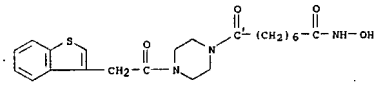
CRN 610801-62-2
CMF C23 H34 N4 O4



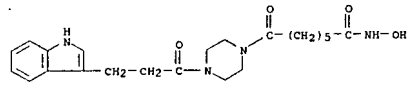
CM 2

CRN 144-62-7
CMF C2 H2 O4

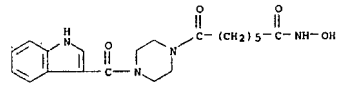
RN 610801-70-2 CAPLUS
CN 1-Piperazineoctanamide, 4-(benzo[b]thien-3-ylacetyl)-N-hydroxy- η-oxo- (9CI) (CA INDEX NAME)



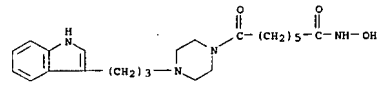
RN 610801-71-3 CAPLUS
CN 1-Piperazineheptanamide, N-hydroxy-4-[3-(1H-indol-3-yl)-1-oxopropyl]-ζ-oxo- (9CI) (CA INDEX NAME)



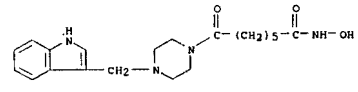
RN 610801-72-4 CAPLUS
CN 1-Piperazineheptanamide, N-hydroxy-4-(1H-indol-3-ylcarbonyl)- ζ-oxo- (9CI) (CA INDEX NAME)



RN 610801-73-5 CAPLUS
CN 1-Piperazineheptanamide, N-hydroxy-4-[3-(1H-indol-3-yl)propyl]- ζ-oxo- (9CI) (CA INDEX NAME)



RN 610801-76-8 CAPLUS
CN 1-Piperazineheptanamide, N-hydroxy-4-(1H-indol-3-ylmethyl)- ζ-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:737742 CAPLUS
DOCUMENT NUMBER: 139:276884
TITLE: Preparation of sulfonyl-derivatives as novel inhibitors of histone deacetylase
INVENTOR(S): Van Emelen, Kristof; Arts, Janine; Backx, Leo Jacobus Jozef; De Winter, Hans Louis Jos; Van Brandt, Sven Franciscus Anna; Verdonck, Marc Gustaaf Celine; Meerpoel, Lieven; Pilatte, Isabelle Noeelle Constance; Poncelet, Virginie Sophie; Dyatkin, Alexey Borisovich
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.; et al.
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076422	A1	20030918	WO 2003-EP2516	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2003218738	A1	20030922	AU 2003-218738	20030311
EP 1485365	A1	20041215	EP 2003-711982	20030311
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CN 1642931	A	20050720	CN 2003-805952	20030311
JP 2005525380	T	20050825	JP 2003-574641	20030311
NZ 534830	A	20050826	NZ 2003-534830	20030311
IN 2004DN02524	A	20070413	IN 2004-DN2524	20040830
US 20051133373	A1	20050526	US 2004-507708	20040913
US 7205304	B2	20070417		
NO 2004004314	A	20041012	NO 2004-4314	20041012
US 2007142393	A1	20070621	US 2007-668906	20070130

PRIORITY APPLN. INFO.:

US 2002-363799P	P	20020313
US 2002-420989P	P	20021024
WO 2003-EP2516	W	20030311
US 2004-507708	A3	20040913

OTHER SOURCE(S): MARPAT 139:276884
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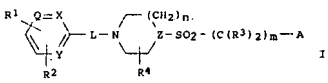
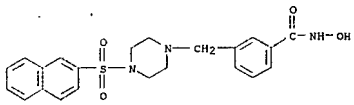


I

AB This invention comprises the novel compds. (I) (wherein n = 1-3, m = 1-4, Q, X, Y = N, CH; Z = N, CH; R1 = (un)substituted amido, acylamido, guandido, and other Zn chelating group, etc.; R2 = H, halo, OH, NH2, NO2, C1-6alkyl, C1-6alkoxy, CF3, di(C1-6alkyl)amino, HONH, naphthalenylsulfonylpyrazinyl; R3 = H aryl; R4 = H, HO, NH2, hydroxyC1-6alkyl, C1-6alkyl, C1-6alkoxy, arylC1-6alkyl, aminocarbonyl, hydroxycarbonyl, aminoC1-6alkyl, aminocarbonylC1-6alkyl, hydroxycarbonylC1-6alkyl, hydroxyaminocarbonyl, C1-6alkoxycarbonyl, C1-6alkylamino, di(C1-6alkyl)aminoC1-6alkyl; L = nul or bivalent radical selected from C1-6alkanediyl, amino, carbonyl or aminocarbonyl; A = aryl, cyclohexyl, heterocyclic derivs.), having histone deacetylase inhibiting enzymic activity, their preparation, compns. containing them and their use as a medicine. For example, 4-(4-(2-naphthylsulfonyl)piperazin-1-yl)-N-hydroxybenzamide in 100% yield was prepared by the hydrogenation of 4-(4-(2-naphthylsulfonyl)piperazin-1-yl)-N-(phenylmethoxy)benzamide (II) in THF by Pd/C as a catalyst. II was prepared from 1,1-dimethylethyl 4-(4-carboxyphenyl)-1-piperazinecarboxylate and O-(phenylmethyl)hydroxylamine hydrochloride in presence of dimethylaminopyridine in CH2Cl2 and diisopropylcarbodiimide, forming 1,1-dimethylethyl 4-[4-[(phenylmethoxy)amino]carbonylphenyl]-1-piperazinecarboxylate which was saponified and subsequently reacted with 2-naphthalenesulfonyl chloride to give the II.

IT 604769-02-0P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonyl derivs. as histone deacetylase inhibitors and antitumor agent for treatment of cancer)

RN 604769-02-0 CAPLUS
CN Benzamide, N-hydroxy-3-[[4-(2-naphthalenylsulfonyl)-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:485895 CAPLUS
DOCUMENT NUMBER: 139:223711
TITLE: Novel inhibitors of procollagen C-Proteinase. Part 2: glutamic acid hydroxamates
AUTHOR(S): Robinson, L. A.; Wilson, D. M.; Delaet, N. G. J.;

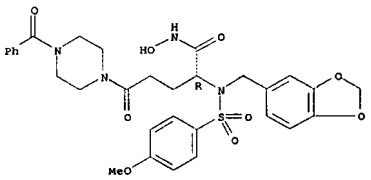
Bradley, E. K.; Dankwardt, S. M.; Campbell, J. A.; Martin, R. L.; Van Wart, H. E.; Walker, K. A. M.; Sullivan, R. W.
CORPORATE SOURCE: CombiChem Inc., San Diego, CA, 92121, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(14), 2381-2384
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:223711

AB Glutamic acid derived hydroxamates were identified as potent and selective inhibitors of procollagen C-proteinase, an essential enzyme for the processing of procollagens to fibrillar collagens. Such compds. have potential therapeutic application in the treatment of fibrosis.

IT 279255-56-0P 279255-58-2P 591766-14-2P
591766-15-3P 591766-16-4P 591766-17-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and structure-activity relationship of glutamic acid hydroxamates as novel inhibitors of procollagen C-Proteinase)

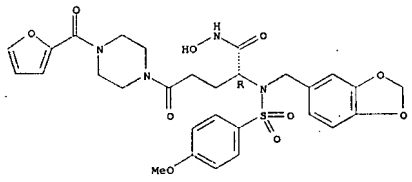
RN 279255-56-0 CAPLUS
CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-4-benzoyl-N-hydroxy- δ-oxo-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



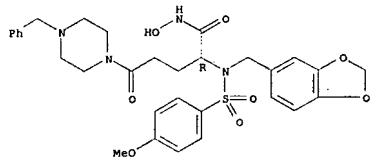
RN 279255-58-2 CAPLUS
CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-4-(2-furanylcarbonyl)-N-hydroxy- δ-oxo-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



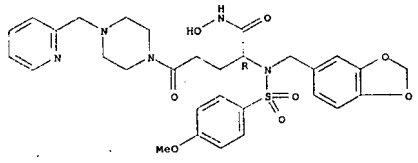
RN 591766-14-2 CAPLUS
CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-N-hydroxy- δ-oxo-4-(phenylmethyl)-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 591766-15-3 CAPLUS
CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-N-hydroxy- δ-oxo-4-(2-pyridinylmethyl)-, (αR)- (9CI) (CA INDEX NAME)

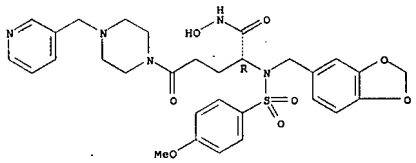
Absolute stereochemistry.



RN 591766-16-4 CAPLUS
CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-

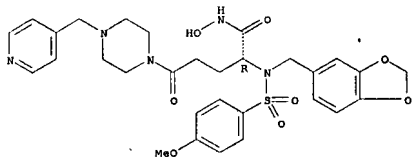
methoxyphenyl)sulfonyl]amino]-N-hydroxy- δ-oxo-4-(3-pyridinylmethyl)-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 591766-17-5 CAPLUS
CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-N-hydroxy- δ-oxo-4-(4-pyridinylmethyl)-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:300644 CAPLUS
DOCUMENT NUMBER: 138:304308
TITLE: Preparation of sulfonyl aryl hydroxamates and their use as matrix metalloprotease inhibitors
INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Decrescenzo, Gary A.; Freskos, John N.; Getman, Daniel P.; McDonald, Joseph J.; Mischke, Brent V.; Rao, Shashidhar N.; Villamil, Clara I.
PATENT ASSIGNEE(S): Pharmacia Corp., USA
SOURCE: U.S. Pat. Appl. Publ., 148 pp., Cont.-in-part of U.S. Ser. No. 569,034.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11

PATENT INFORMATION:

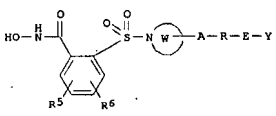
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003073845	A1	20030417	US 2001-909227	20010719
US 6696449	B2	20040224		
WO 9838859	A1	19980911	WO 1998-US4300	19980304
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, GM, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 2001020021	A1	20010906	US 1999-230209	19990624
US 6380258	B2	20020430		
US 7115632	B1	20061003	US 2000-569034	20000511
US 2003191317	A1	20031009	US 2000-728408	20001201
US 6794511	B2	20040921		
CA 2453613	A1	20030130	CA 2002-2453613	20020719
WO 2003007954	A2	20030130	WO 2002-US23219	20020719
WO 2003007954	A3	20031023		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002326432	A1	20030303	AU 2002-326432	20020719
EP 1406626	A2	20040414	EP 2002-761148	20020719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011430	A	20040713	BR 2002-11430	20020719
JP 2005502632	T	20050127	JP 2003-513561	20020719

PRIORITY APPLN. INFO.:

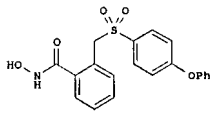
US 1997-35182P	P	19970304
WO 1998-US4300	W	19980304
US 1999-310813	B2	19990512
US 1999-230209	A2	19990624
US 2000-569034	A2	20000511
US 2000-728408	A2	20001201
US 2001-909227	A	20010719
WO 2002-US23219	W	20020719

OTHER SOURCE(S): MARPAT 138:304308

GI



I



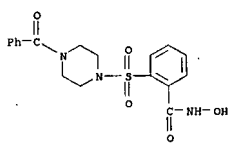
II

AB Title compds. I [W = 6-membered heterocycle containing the sulfonyl bonded N; A-R-E-Y = 4-substituent; A = O, SO0-2, etc.; R = alkyl, alkoxyalkyl, aryl, heteroaryl, cycloalkyl, etc.; E = absent , bond, CO, SO2, etc.; Y = absent, H, OH, CN, NO2, alkyl, haloalkyl, aminoalkyl; R5-6 = together with the atoms to which they are bonded, form an aliphatic or aromatic carbocyclic or heterocyclic ring having 5-7 members] are prepared Over 50 synthetic examples are disclosed. For example, phthalide is reacted with 4-(phenoxy)benzenethiol (DMF, K2CO3, 100°C, 2 h) and the resulting product converted to the hydroxamic acid (CH2Cl2, ClCOCOCl, DMF (cat), TMSONH2, 0°C, 1.5 h) followed by oxidation (CH2Cl2, mCPBA, room temperature, 3 h) to II. II has IC50 = 10 nM for MMP-2, 45 nM for MMP-13 and >10,000 nM for MMP-1. I are inhibitors of MMP and angiogenesis.

IT 308385-85-5P 308385-86-6P 308385-87-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of sulfonyl aryl or heteroaryl hydroxamic acids and derivs. as aggrecanase inhibitors)

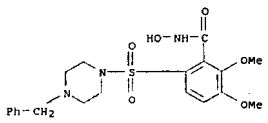
RN 308385-85-5 CAPLUS

CN Benzamide, 2-[(4-benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



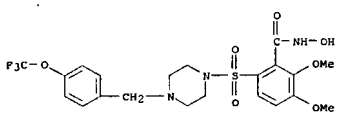
RN 308385-86-6 CAPLUS

CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 308385-87-7 CAPLUS

CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-[[4-(trifluoromethoxy)phenyl]methyl]-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:76616 CAPLUS

DOCUMENT NUMBER: 138:117647

TITLE: Sulfonyl aryl hydroxamates and their use as matrix metalloprotease inhibitors

INVENTOR(S): McDonald, Joseph J.; Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Rao, Shashidhar N.; Freskos, John N.; De Crescenzo, Gary A.; Mischke, Brent V.; Getman, Daniel P.; Villamil, Clara I.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA; et al.

SOURCE: PCT Int. Appl., 214 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 11

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003007954	A2	20030130	WO 2002-US23219	20020719
WO 2003007954	A3	20031023		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003073845	A1	20030417	US 2001-909227	20010719
US 6696449	B2	20040224		
CA 2453613	A1	20030130	CA 2002-2453613	20020719
AU 2002326432	A1	20030303	AU 2002-326432	20020719
EP 1406626	A2	20040414	EP 2002-761148	20020719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011430	A	20040713	BR 2002-11430	20020719
JP 2005502632	T	20050127	JP 2003-513561	20020719

PRIORITY APPLN. INFO.:

US 2001-909227	A	20010719
US 1997-35182P	P	19970304
WO 1998-US4300	W	19980304
US 1999-310813	B2	19990512
US 1999-230209	A2	19990624
US 2000-569034	A2	20000511
US 2000-728408	A2	20001201
WO 2002-US23219	W	20020719

OTHER SOURCE(S): MARPAT 138:117647

AB The invention discloses sulfonyl aromatic hydroxamic acid compds. and salts thereof that, inter alia, inhibit matrix metalloprotease (MMP) activity and/or aggrecanase activity. The invention also is directed to a process that comprises administering such a compound or pharmaceutically acceptable salt thereof to a host animal having a condition associated with MMP activity.

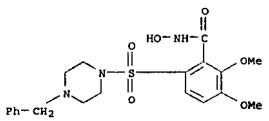
IT 308385-85-5P 308385-86-6P 308385-87-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of sulfonyl aryl or heteroaryl hydroxamic acids and derivs. as aggrecanase inhibitors)

RN 308385-85-5 CAPLUS

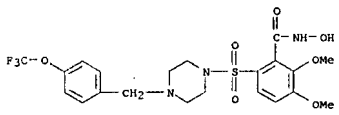
CN Benzamide, 2-[(4-benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)

RN 308385-86-6 CAPLUS

CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 308385-87-7 CAPLUS
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-[[4-(trifluoromethoxy)phenyl]meth yl]-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)

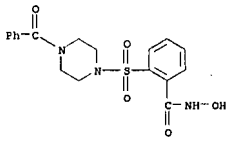


L4 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:76594 CAPLUS
DOCUMENT NUMBER: 138:117646
TITLE: Use of sulfonyl aryl or heteroaryl hydroxamic acids and derivatives as aggrecanase inhibitors
INVENTOR(S): McDonald, Joseph J.; Barta, Thomas A.; Arner, Elizabeth; Boehm, Terri L.; Becker, Daniel P.; Decrescenzo, Gary A.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 274 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

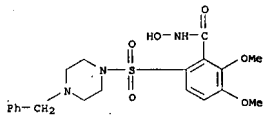
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003007930	A2	20030130	WO 2002-US22867	20020719
WO 2003007930	A3	20030821		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003171404	A1	20030911	US 2002-194897	20020712
US 6683078	B2	20040127		

CA 2453602	A1	20030130	CA 2002-2453602	20020719
AU 2002327264	A1	20030303	AU 2002-327264	20020719
EP 1406602	A2	20040414	EP 2002-763298	20020719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011210	A	20040713	BR 2002-11210	20020719
JP 2005504026	T	20050210	JP 2003-513538	20020719
PRIORITY APPLN. INFO.:			US 2001-306629P	P 20010719
			WO 2002-US22867	W 20020719

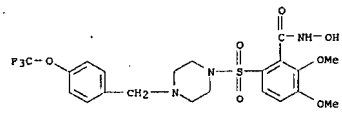
OTHER SOURCE(S): MARPAT 138:117646
AB The invention discloses a process for inhibiting aggrecanase activity. The process comprises administering a therapeutically effective amount of a sulfonyl aromatic or heteroarom. hydroxamic acid, a derivative thereof, or a pharmaceutically acceptable salt of the hydroxamic acid or derivative to a host animal.
IT 308385-85-5P 308385-86-6P 308385-87-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of sulfonyl aryl or heteroaryl hydroxamic acids and derivs. as aggrecanase inhibitors)
RN 308385-85-5 CAPLUS
CN Benzamide, 2-[(4-benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 308385-86-6 CAPLUS
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 308385-87-7 CAPLUS
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-[[4-(trifluoromethoxy)phenyl]meth yl]-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)

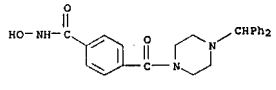


L4 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:43028 CAPLUS
DOCUMENT NUMBER: 138:106596
TITLE: Preparation of thiophenedicarboxamides and related compounds as histone deacetylase (HDAC) inhibitors.
INVENTOR(S): Leser-Reiff, Ulrike; Sattelkau, Tim; Zimmermann, Gerd
PATENT ASSIGNEE(S): Hoffman-La Roche, Inc., Germany
SOURCE: U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003013757	A1	20030116	US 2002-167677	20020611
US 6784173	B2	20040831		
CA 2449804	A1	20030213	CA 2002-2449804	20020613
WO 2003011851	A2	20030213	WO 2002-EP6488	20020613
WO 2003011851	A3	20030918		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002355626	A1	20030217	AU 2002-355626	20020613
EP 1401824	A2	20040331	EP 2002-791436	20020613
EP 1401824	B1	20061025		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1516697	A	20040728	CN 2002-812010	20020613
BR 2002010424	A	20040817	BR 2002-10424	20020613
NZ 529874	A	20041224	NZ 2002-529874	20020613
JP 2005502641	T	20050127	JP 2003-517043	20020613
AT 343569	T	20061115	AT 2002-791436	20020613
RU 2289560	C2	20061220	RU 2003-137578	20020613
ZA 2003009260	A	20050228	ZA 2003-9260	20031127
IN 2003CN01981	A	20060106	IN 2003-CN1981	20031211
BG 108450	A	20050131	BG 2003-108450	20031215
US 2004214862	A1	20041028	US 2004-847166	20040517
HK 1065787	A1	20061117	HK 2004-108497	20041029
PRIORITY APPLN. INFO.:			EP 2001-114496	A 20010615

			US 2002-167677	A3 20020611
			WO 2002-EP6488	W 20020613

OTHER SOURCE(S): MARPAT 138:106596
AB HONHCOACONR1R2 [A = (substituted) Ph, thienyl; R1, R2 = H, (substituted) alkyl, carbocyclyl, heterocyclyl; NR1R2 = (substituted) 3-6 membered ring], were prepared Thus, thiophene-2,5-dicarboxylic acid monomethyl ester and N-methylmorpholine in CH2Cl2 at -10° were treated with 1-aminomethylnaphthalene in CH2Cl2; the mixture was stirred 90 min to give 58% monoamide. This was stirred with NH2OH.HCl and NaOMe in MeOH for 4 h to give thiophene-2,5-dicarboxylic acid 2-hydroxyamide 5-[(naphthalen-1-ylmethyl)amide]. Tested title compds. inhibited HT-29 tumor cell growth with IC50 = 0.02-0.17 μM. A tablet formulation is given.
IT 487004-50-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of thiophenedicarboxamides and related compds.
as histone deacetylase (HDAC) inhibitors)
RN 487004-50-2 CAPLUS
CN Benzamide, 4-[[4-(diphenylmethyl)-1-piperazinyl]carbonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

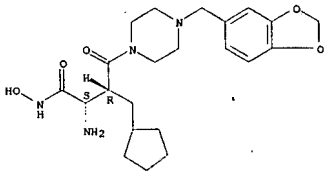
L4 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:319307 CAPLUS
DOCUMENT NUMBER: 137:75137
TITLE: Predictions of Binding of a Diverse Set of Ligands to Gelatinase-A by a Combination of Molecular Dynamics and Continuum Solvent Models
AUTHOR(S): Hou, Tingjun; Guo, Senli; Xu, Xiaojie
CORPORATE SOURCE: College of Chemistry and Molecular Engineering, Peking University, Beijing, 100871, Peop. Rep. China
SOURCE: Journal of Physical Chemistry B (2002), 106(21), 5527-5535
CODEN: JPCBFK; ISSN: 1089-5647
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The free energies of binding, ΔGbind, between a diverse set of eight hydroxamate inhibitors with gelatinase-A (MMP-2) were computed by using the recently developed MM/PBSA approach. In this paper, a nonbonded model was used to represent the potentials of the catalytic zinc center. Mol. dynamics (MD) simulations were used to generate the thermally averaged ensemble of conformations of the ligand-protein complexes. On the basis of the trajectories from MD simulations, the free energies of binding were calculated using mol. mechanics, the continuum solvent model, surface area

estimation, and normal-mode anal. The results show that MM/PBSA not only can rank the studied ligands effectively but also can reproduce the exptl. binding free energies successfully. The predicted binding free energies correlate well with the exptl. values (r = 0.84, q = 0.78). As a comparison, the free energies of binding were also computed by using the linear interaction energy approximation (LIE). The overall agreement between the calculated and exptl. values for the diverse set of ligands means that the MM/PBSA approach is a useful tool for the general evaluation of protein-ligand interactions. The anal. of the sep. energy terms contributing to MM/PBSA free energy indicates that the association between hydroxamate and MMP-2 is mainly driven by more favorable van der Waals/nonpolar interactions in the complex than in solution

IT 220046-45-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(linear interaction energy approximation reveals association between hydroxamate and MMP-2 is promoted by van der Waals/nonpolar interactions in complex than in solution)

RN 220046-45-7 CAPLUS
CN 1-Piperazinebutanamide, α-amino-4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy- γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:275960 CAPLUS
DOCUMENT NUMBER: 136:310184
TITLE: Preparation of hydroxamic acid peptide deformylase inhibitors as antibacterial agents
INVENTOR(S): Chong, Lee; Frechette, Roger; Scott, Carole; Tester, Richard; Smith, Whitney; Chiba, Katsumi; Sakamoto, Masatoshi; Gluchowski, Charles
PATENT ASSIGNEE(S): Questcor Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 171 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028829	A2	20020411	WO 2001-US29926	20010924
WO 2002028829	A3	20031224		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002030385	A5	20020415	AU 2002-30385	20010924
PRIORITY APPLN. INFO.:			US 2000-234967P	P 20000925
			US 2001-761850	A 20010118
			WO 2001-US29926	W 20010924

OTHER SOURCE(S): MARPAT 136:310184
GI

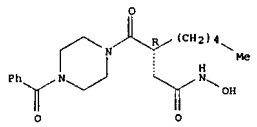
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Hydroxamic acid derivs. of peptides and peptidomimetics of formulas I, II, and III [wherein Z = NHOH or ORa; Ra = alkyl or a bioclеavable moiety; X = CO or SO2; Y = (un)substituted heteroalkyl or heterocyclyl; R1 = (un)substituted (cyclo)alkyl, aryl, heterocyclyl, or heteroalkyl; R2R3 = 4-7 membered (un)substituted heterocycle; R2R4 = ring formed through a CH2CH2 linkage; or R2 = Me; or R3 = H or (un)substituted (hetero)alkyl, aryl, or heterocyclyl; or R4 = H or (un)substituted (hetero)alkyl, aryl, or heterocyclyl; R5 and R6 = independently H, NO2, NH2, NHCOH, NHCOCH3, NHSO2CH3, or (un)substituted CH2NH-(hetero)alkyl or CH2NH-heterocyclyl; one of R7 or R8 = CHR10CONHOH; one of R7 or R8 = (un)substituted (hetero)alkyl, (alkyl)heterocyclyl, or alkylaryl; R9 and R10 = independently H or (un)substituted (hetero)alkyl, (alkyl)heterocyclyl, or alkylaryl] were prepared as peptide deformylase (Fe-PDF) inhibitors for treating various bacterial infections. For example, 3-pyrrolidinol was added to tert-Bu (R)-(2-pentyl)succinate mono(N-hydroxysuccinimide) ester to give the amide (68%). Treatment with 20% TFA/DCM, followed by MeOH, benzene, and TMSN2 in hexanes, to afford the Me ester (90%). The pyrrolidinol was coupled with 4-methoxyphenylisocyanate and the ester converted to the hydroxamic acid (IV) using NH2OH•HCl. The latter inhibited E. coli Fe-PDF with IC50 of 9 nM and showed selectivity for Fe-PDF vs. thermolysin with a selectivity index of 30,000. Thus, I, II, and III are useful as antibiotics against a broad range of infectious disease in animals and humans.

IT 409129-95-9P 409129-96-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptide deformylase inhibitor; preparation of hydroxamic acid derivs. of peptides and peptidomimetics as peptide deformylase inhibitors for treatment of infectious diseases)

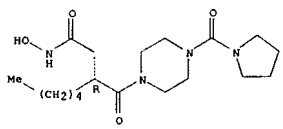
RN 409129-95-9 CAPLUS
CN 1-Piperazinebutanamide, 4-benzoyl-N-hydroxy-γ-oxo-β-pentyl-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 409129-96-0 CAPLUS
CN 1-Piperazinebutanamide, N-hydroxy-γ-oxo-β-pentyl-4-(1-pyrrolidinylcarbonyl)-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

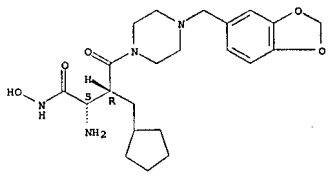


L4 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:161702 CAPLUS
DOCUMENT NUMBER: 137:5788
TITLE: Binding free energy calculations for MMP2-hydroxamate complexes
AUTHOR(S): Hou, Ting-Jun; Zhang, Wei; Xu, Xiao-Jie
CORPORATE SOURCE: College of Chemistry and Molecular Engineering, Peking University, Beijing, 100871, Peop. Rep. China
SOURCE: Huaxue Xuebao (2002), 60(2), 221-227
CODEN: HHHPA4; ISSN: 0567-7351
PUBLISHER: Kexue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The absolute binding affinities of hydroxamate inhibitors with MMP-2 were evaluated by mol. dynamics (MD) simulations with a linear response approach. During MD simulations, a nonbonded model for the catalytic Zn center was used to represent the interactions between Zn center and enzyme/inhibitor. The trajectories from MD simulation show that using the nonbonded model the catalytic Zn ion adopts five coordination number, but the coordination form exists large difference with that of the initial model. After fittings, the models with one parameter, two parameters and three parameters were obtained. The calculated results indicate that the three-parameter model with a constant term bears the best predicting ability. The best model yields an average error of 2.38 kJ/mol for the eight binding affinities of hydroxamates.
IT 220046-45-7
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL

(Biological study)
(binding free energy calcns. for MMP2-hydroxamate complexes)

RN 220046-45-7 CAPLUS
CN 1-Piperazinebutanamide, α-amino-4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy- γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:833270 CAPLUS
DOCUMENT NUMBER: 135:371526
TITLE: Preparation of sulfonyl aryl or heteroaryl hydroxamic acid compounds as inhibitors of matrix metalloproteinase
INVENTOR(S): Bedell, Louis J.; Mconald, Joseph; Barta, Thomas E.; Becker, Daniel P.; Rao, Shashidhar N.; Freskos, John N.; Mischke, Brent V.; Getman, Daniel P.; Decrescenzo, Gary A.; Villamil, Clara I.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 374 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085680	A2	20011115	WO 2001-US14706	20010507
WO 2001085680	A3	20020307		

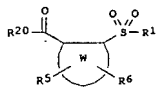
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 7115632	B1	20061003	US 2000-569034	20000511
PRIORITY APPLN. INFO.:			US 2000-569034	A 20000511
			US 1999-310813	B2 19990512

US 1999-230209 A2 19990624

OTHER SOURCE(S): MARPAT 135:371526

GI



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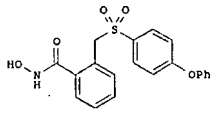


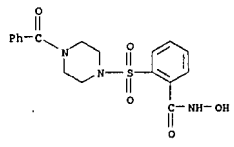
II

AB Title compds. I [W = 5-, 6-membered aromatic or heteroarom. ring; R1 = a substituent containing a 5- or 6-membered cyclohydrocarbyl, heterocyclo, aryl or heteroaryl radical that is bonded directly to the depicted SO2-group said R1 with certain steric requirements; R5-6 = H, alkyl, cycloalkyl, acylalkyl, halo, nitro, hydroxy, cyano, alkoxy, haloalkyl, haloalkyloxy, hydroxyalkyl, etc. or R5-6 together with the atoms to which they are bonded form a further aliphatic or aromatic carbocyclic or heterocyclic ring having 5-to 7-members; R20 = OR21, where R21 = H, alkyl, aryl, arylalkyl, NR13OR22, where R22 = a selectively removable protecting group and R13 = H, alkyl, benzyl group, etc.] were prepared Over 50 synthetic examples were disclosed. For example, phthalide was reacted with 4-(phenoxy)benzenethiol (DMF, K2CO3, 100°C, 2 h) and the resulting product converted to the hydroxamic acid (CH2Cl2, ClCOCOCl, DMF (cat), TMSONH2,0°C, 1.5 h) followed by oxidation (CH2Cl2, mCPBA, room temperature, 3 h) to II. II had IC50 = 10 nM for MMP-2, 45 nM for MMP-13 and >10,000 nM for MMP-1. I are inhibitors of MMP and angiogenesis.

IT 308385-85-5P, 2-[(4-Benzoyl-1-piperazinyl)sulfonyl]-N-hydroxybenzamide 373367-17-0P, N-Hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]benzamide hydrochloride 373367-18-1P, N-Hydroxy-2,3-dimethoxy-6-[[4-[(4-(trifluoromethoxy)phenyl]methyl]-1-piperazinyl]sulfonyl]benzamide hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; preparation of sulfonyl aryl or heteroaryl hydroxamic acid compds. as inhibitors of matrix metalloproteinase)

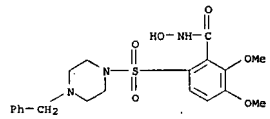
RN 308385-85-5 CAPLUS

CN Benzamide, 2-[(4-benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 373367-17-0 CAPLUS

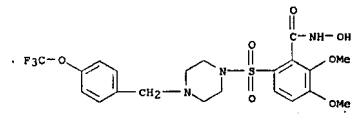
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 373367-18-1 CAPLUS

CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-[(4-(trifluoromethoxy)phenyl]methyl]-1-piperazinyl]sulfonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:472692 CAPLUS

DOCUMENT NUMBER: 135:61355

TITLE: Preparation of α-arylethylpiperazine derivatives as neurokinin antagonists

INVENTOR(S): Stiernet, Francoise; Genicot, Christophe; Lassoie,

Marie-agnes; Moureau, Florence; Ryckmans, Thomas; Taverne, Thierry; Henichart, Jean-pierre; Neuwels, Michel; Goldstein, Solo

PATENT ASSIGNEE(S): Ucb, S.A., Belg.

SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

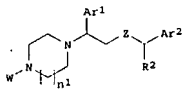
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001046167	A1	20010628	WO 2000-EP12667	20001214
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1110958	A1	20010627	EP 1999-125359	19991220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1242399	A1	20020925	EP 2000-989974	20001214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518108	T	20030603	JP 2001-547078	20001214
US 2003220323	A1	20031127	US 2002-168331	20020830
US 6916797	B2	20050712		

PRIORITY APPLN. INFO.: EP 1999-125359 A 19991220
WO 2000-EP12667 W 20001214

OTHER SOURCE(S): MARPAT 135:61355

GI



I

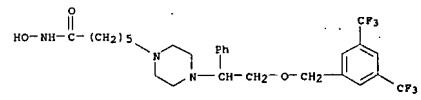
AB The title compds. [I; Z = O, S; n1 = 1-2; R2 = H, Me; W = cyclohexyl substituted by a CO2H, 2-phenylacetic acid, or alkyl 2-phenylacetate, etc.; Ar1 = (un)substituted Ph, aryl, heteroaryl, etc.; Ar2 = (un)substituted Ph, etc.] and their salts, useful as neurokinin receptor antagonists (NK1antagonists), were prepared Thus, hydrolysis of the corresponding Et ester afforded I [Z = O; R2 = H; n1 = 1; W = (CH2)4CO2H; Ar1 = Ph; Ar2 = 3,5-(F3C)2C6H3] which showed pIC50 of 7.5 against binding to NK1 receptors. The compds. I are useful for the prevention and/or treatment of a condition associated with pathol. levels of substance P.

IT 346416-43-1P 346416-44-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of α-arylethylpiperazine derivs. as neurokinin antagonists)

RN 346416-43-1 CAPLUS

CN 1-Piperazinehexanamide, 4-[2-[[3,5-bis(trifluoromethyl)phenyl]methoxy]-1-phenylethyl]-N-hydroxy- (9CI) (CA INDEX NAME)

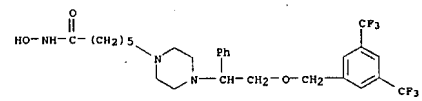


RN 346416-44-2 CAPLUS

CN 1-Piperazinehexanamide, 4-[2-[[3,5-bis(trifluoromethyl)phenyl]methoxy]-1-phenylethyl]-N-hydroxy-, (2Z)-2-butenedioate (1:2) (salt) (9CI) (CA INDEX NAME)

CM 1

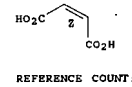
CRN 346416-43-1
CMF C27 H33 F6 N3 O3



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:390470 CAPLUS

DOCUMENT NUMBER: 135:104175

TITLE: Binding Affinities for a Series of Selective

Inhibitors of Gelatinase-A Using Molecular Dynamics with a Linear Interaction Energy Approach

AUTHOR(S): Hou, T. J.; Zhang, W.; Xu, X. J.
CORPORATE SOURCE: College of Chemistry and Molecular Engineering, Peking University, Beijing, 100871, Peop. Rep. China

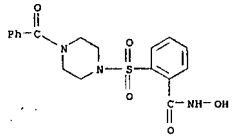
SOURCE: Journal of Physical Chemistry B (2001), 105(22), 5304-5315
CODEN: JPCBFK; ISSN: 1089-5647
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The binding of a series of hydroxamate inhibitors with gelatinase-A is examined to evaluate the viability of calculating free energies of binding, ΔGb, utilizing mol. dynamics (MD) simulations with a linear interaction energy approach. In our simulations, a bonded model was used to represent the potentials of the catalytic zinc center. The electrostatic distribution of this model was derived using a two-stage electrostatic potential fitting calcns. The resulting bonded model was then used to generate the MD trajectories. Coulombic, van der Waals, and coordinate bond energy components determined from MD simulations of the bound and unbound inhibitors solvated in water were correlated with the free energies of binding for the 15 hydroxamate inhibitors. In the correlation process, several linear models consisted of different energy components were tested. We found that besides the usually used Coulombic and van der Waals energy terms, the introduction of a constant term could significantly improve the correlation. The best model yields an average error of 0.6 kcal/mol for the 15 binding affinities, which cover an observed range of 7.2 kcal/mol. The predictive ability of the best model was revealed by the high value of q2 (0.854) from the leave-one-out cross-validation. To this series of inhibitors, the constant term can be treated as effective adjustment to the entropy contribution in the binding free energies. The MD simulations predicted the binding mode of the gelatinase-A with the studied inhibitors, and also provided insights into the interactions occurring in the active site and the origins of variations in ΔGb. The P1' groups of inhibitors make extensive van der Waals and hydrophobic contacts with the nonpolar side chains of four residues in the S1' subsite, including Leu 197, Val 198, Leu 218, and Tyr 223, which directly influence the ligand binding. Hydrogen bonds between hydroxamates and gelatinase-A are very important to stabilize the inhibitors in the active site. The hydrogen bonds between the P3' group and gelatinase-A can produce more favorable electrostatic interactions.

IT 220046-45-7
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(binding affinities for a series of selective inhibitors of gelatinase-A using mol. dynamics with a linear interaction energy approach)

RN 220046-45-7 CAPLUS
CN 1-Piperazinebutanamide, α-amino-4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy- γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

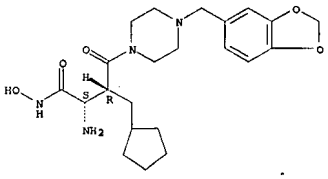


REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:824218 CAPLUS
DOCUMENT NUMBER: 134:4752
TITLE: Preparation of hydroxamic acid derivatives as matrix metalloprotease inhibitors
INVENTOR(S): Bedell, Louis J.; McDonald, Joseph J.; Barta, Thomas E.; Becker, Daniel P.; Rao, Shashidhar N.; Freskos, John N.; Mischke, Brent V.; Getman, Daniel P.; Decrescenzo, Gary A.; Villamil, Clara I.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 380 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000069819	A1	20001123	WO 2000-US6713	20000512
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2373500	A1	20001123	CA 2000-2373500	20000512
EP 1177173	A1	20020206	EP 2000-931910	20000512
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000011291	A	20020514	BR 2000-11291	20000512
JP 2002544257	T	20021224	JP 2000-618236	20000512
NZ 515197	A	20040326	NZ 2000-515197	20000512
AU 781339	B2	20050519	AU 2000-49718	20000512
ZA 2001009007	A	20030131	ZA 2001-9007	20011031
PRIORITY APPLN. INFO.:			US 1999-310813 A	19990512
			WO 2000-US6713 W	20000512

OTHER SOURCE(S): MARPAT 134:4752
GI



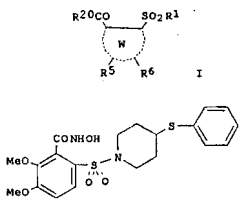
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:853658 CAPLUS
DOCUMENT NUMBER: 134:222499
TITLE: Synthesis and activity of selective MMP inhibitors with an aryl backbone
AUTHOR(S): Barta, T. E.; Becker, D. P.; Bedell, L. J.; De Crescenzo, G. A.; McDonald, J. J.; Munie, G. E.; Rao, S.; Shieh, H.-S.; Stegeman, R.; Stevens, A. M.; Villamil, C. I.
CORPORATE SOURCE: Pharmacia, Department of Medicinal Chemistry, Skokie, IL, 60077, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(24), 2815-2817
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:222499

AB A series of novel, MMP-1 sparing arylhydroxamate sulfonamides with activity against MMP-2 and MMP-13 is described. Example compds. thus tested were N-hydroxy-2-[[(phenylmethyl)amino]sulfonyl]benzamide, N-hydroxy-2-[[(4-methoxyphenyl)methylamino]sulfonyl]benzamide, N-hydroxy-2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]benzamide, 2-fluoro-N-hydroxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide, and derivs. or homologs thereof. The crystal and mol. structure of 2-fluoro-N-hydroxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide compound with MMP-8 were reported.

IT 308385-85-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
((aminosulfonyl)-N-hydroxybenzamide derivs. and their activity as gelatinase (MMP-2) and collagenase (MMP-13) inhibitors)

RN 308385-85-5 CAPLUS
CN Benzamide, 2-[(4-benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)

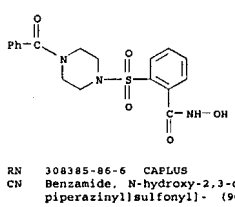


II

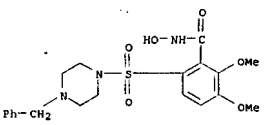
AB Title compds. [I; W = 5, 6 membered aromatic, heteroarom. ring; R = 5, 6 membered cyclohydrocarbyl, heterocyclo, aryl, heteroaryl; R5, R6 independently = hydrido, alkyl, cycloalkyl, acylalkyl, halo, nitro, hydroxyl, cyano, alkoxy, haloalkyl, haloalkyloxy, hydroxyalkyl, etc; R20 = alkoxy, aryloxy, alkoxyamino, benzyloxyamino, etc] and pharmaceutically acceptable salts with inter alia inhibits matrix metalloprotease activity are disclosed and a treatment that comprises administering a contemplated sulfonyl aromatic or heteroarom. hydroxamic acid in an MMP enzyme-inhibiting effective amount to a host having a condition associated with pathol. matrix metalloprotease activity are claimed. Thus, the title compound II was prepared and MMP-2, MMP-3, MMP-8, MMP-13, and MT1-MMP inhibition activities were assayed.

IT 308385-85-5P 308385-86-6P 308385-87-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hydroxamic acid derivs. as matrix metalloprotease inhibitors)

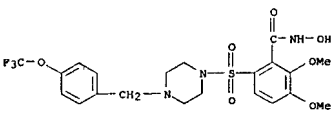
RN 308385-85-5 CAPLUS
CN Benzamide, 2-[(4-benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 308385-86-6 CAPLUS
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 308385-87-7 CAPLUS
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-[[4-(trifluoromethoxy)phenyl]methyl]-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

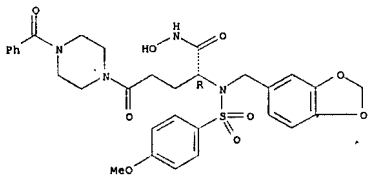
L4 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:441768 CAPLUS
DOCUMENT NUMBER: 133:74324
TITLE: Preparation of amino acid sulfonamide hydroxamates as inhibitors of procollagen C-proteinase.
INVENTOR(S): Billedeau, Roland Joseph; Broka, Chris Allen; Campbell, Jeffrey Allen; Chen, Jian Jeffrey; Dankwardt, Sharon Marie; Delaet, Nancy; Robinson, Leslie Ann; Walker, Keith Adrian Murray
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037436	A1	20000629	WO 1999-EP9920	19991214
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2355902	A1	20000629	CA 1999-2355902	19991214
BR 9916504	A	20010911	BR 1999-16504	19991214

EP 1149072	A1	20011031	EP 1999-963530	19991214
EP 1149072	B1	20040630		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200101868	T2	20011121	TR 2001-200101868	19991214
HU 200104658	A2	20020629	HU 2001-4658	19991214
JP 2002533322	T	20021008	JP 2000-589508	19991214
AU 769319	B2	20040122	AU 2000-19792	19991214
NZ 512292	A	20040326	NZ 1999-512292	19991214
AT 270271	T	20040715	AT 1999-963530	19991214
RU 2232751	C2	20040720	RU 2001-119461	19991214
US 6492394	B1	20021210	US 1999-469660	19991222
HR 2001000443	A1	20020630	HR 2001-443	20010614
ZA 2001005014	A	20020919	ZA 2001-5014	20010619
MX 2001PA06328	A	20010910	MX 2001-PA6328	20010620
IN 2001CN00859	A	20050304	IN 2001-CN859	20010620
NO 2001003100	A	20010821	NO 2001-3100	20010621
US 2003199520	A1	20031023	US 2002-267292	20021009
US 6844366	B2	20050118		
US 2003216405	A1	20031120	US 2002-267727	20021009
US 6787559	B2	20040907		
PRIORITY APPLN. INFO.:			US 1998-113311P	P 19981222
			US 1999-147053P	P 19990803
			US 1999-164138P	P 19991108
			WO 1999-EP9920	W 19991214
			US 1999-469660	A3 19991222

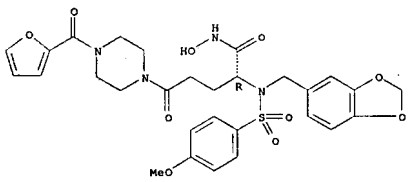
OTHER SOURCE(S): MARPAT 133:74324
AB HOHNCOCHR1NRSO2Ar2 [R1 = alkyl, haloalkyl, heteroalkyl, cycloalkyl, aryl, aralkyl, aralkenyl, heteroaryl, heteroaralkyl, amin1, aryl, aralkyl, etc.; R = CHR2Ar1, CHR2CH:CHAr1; Ar2 = specified (substituted) Ph, naphthyl; R2 = H, alkyl; with provisos], were prepared Thus, N-hydroxy-2(R)-[(3,4-methylenedioxybenzyl)(4-methoxy-2,3,6-trimethylbenzenesulfonyl)amino]-3-methylbutyramide was prepared by solution phase synthesis from BOC-D-Val-OH. Title compds. inhibited procollagen C-proteinase with IC50 0.01-2 μM.
IT 279255-56-0P 279255-58-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid sulfonamide hydroxamates as inhibitors of procollagen C-proteinase)
RN 279255-56-0 CAPLUS
CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-4-benzoyl-N-hydroxy- δ-oxo-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 279255-58-2 CAPLUS
CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-4-(2-furanylcarbonyl)-N-hydroxy- δ-oxo-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



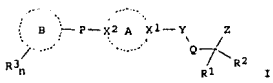
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:161258 CAPLUS
DOCUMENT NUMBER: 132:207849
TITLE: Preparation of arylpiperazines as metalloproteinase inhibiting agents (MMP)
INVENTOR(S): Barlaam, Bernard Christophe; Newcombe, Nicholas John; Tucker, Howard; Waterson, David
PATENT ASSIGNEE(S): Zeneca Limited, UK; Zeneca-Pharma Sa
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012478	A1	20000309	WO 1999-GB2801	19990825
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,				

CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2339761	A1	20000309	CA 1999-2339761	19990825
AU 9955247	A	20000321	AU 1999-55247	19990825
AU 764367	B2	20030814		
BR 9913255	A	20010522	BR 1999-13255	19990825
EP 1109787	A1	20010627	EP 1999-941751	19990825
EP 1109787	B1	20060517		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
TR 200100605	T2	20010821	TR 2001-200100605	19990825
HU 200103344	A2	20020228	HU 2001-3344	19990825
EE 200100106	A	20020617	EE 2001-106	19990825
JP 2002523493	T	20020730	JP 2000-567511	19990825
NZ 509730	A	20030530	NZ 1999-509730	19990825
RU 2220967	C2	20040110	RU 2001-108591	19990825
NZ 524921	A	20041029	NZ 1999-524921	19990825
AT 326448	T	20060615	AT 1999-941751	19990825
PT 1109787	T	20060929	PT 1999-941751	19990825
ES 2263284	T3	20061201	ES 1999-941751	19990825
TW 240722	B	20051001	TW 1999-88114833	19990830
ZA 2001001231	A	20020513	ZA 2001-1231	20010213
MX 2001PA01847	A	20020408	MX 2001-PA1847	20010220
US 6734184	B1	20040511	US 2001-763709	20010226
NO 2001001023	A	20010425	NO 2001-1023	20010228
NO 321478	B1	20060515		
BG 105369	A	20011231	BG 2001-105369	20010322
HK 1036060	A1	20061027	HK 2001-106732	20010924
AU 2003262101	A1	20031218	AU 2003-262101	20031112
US 2004171641	A1	20040902	US 2004-787775	20040226
PRIORITY APPLN. INFO.:			EP 1998-402144	A 19980831
			EP 1999-401351	A 19990604
			WO 1999-GB2801	W 19990825
			US 2001-763709	A1 20010226

OTHER SOURCE(S): MARPAT 132:207849
GI



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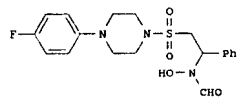


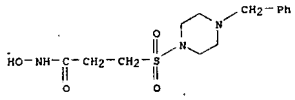
II

AB The title compds. [I; B = monocyclic or bicyclic alkyl, aryl, etc.; R3 = H, halo, NO2, etc.; n = 1-3; P = (CH2)n (wherein n = 0-2), alkene, alkyne, etc.; A = (un)substituted 5-7 membered aliphatic ring; X1, X2 = N, C, where a ring substituent on ring A is a oxo group that is preferably adjacent a ring N atom; Y = SO2, CO; Z = CONHOH, Y = CO and Q = CR6R7, CR6R7CH2, NR6, NR6CH2 (wherein R6 = H, alkyl, aralkyl, etc.; R7 = H, alkyl; R7 together with R6 forms a carbocyclic or heterocyclic spiro 5-7 membered ring, the latter containing at least one heteroatom selected from N, O, S); Z = CONHOH, Y = SO2 and Q = CR6R7, CR6R7CH2; Z = N(OH)CHO and Q = CHR6, CHR6CH2, NR6CH2; R1 = H, alkyl, cycloalkyl, etc.; R2 = H, alkyl, aryl, etc.], useful as metalloproteinase inhibitors (no data), especially as inhibitors of MMP 13, in treating arthritis and atherosclerosis, were prepared. E.g., a multi-step synthesis of the title piperazine II was given. Compds. I are effective at 0.5-30 mg/kg/day.

IT 260438-45-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylpiperazines as metalloproteinase inhibiting agents (MMP))

RN 260438-45-7 CAPLUS

CN Propanamide, N-hydroxy-3-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (CA INDEX NAME)



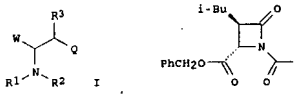
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:64787 CAPLUS
DOCUMENT NUMBER: 130:139360

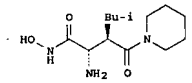
TITLE: Preparation of succinyl piperidinamides, morpholinamides, piperazinamides, and analogs as matrix metalloproteinase inhibitors
INVENTOR(S): Alpegiani, Marco; Bissolino, Pierluigi; Abrate, Francesca; Perrone, Ettore; Corigli, Riccardo; Jabes, Daniela
PATENT ASSIGNEE(S): Pharmacia & Upjohn S.P.A., Italy
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902510	A1	19990121	WO 1998-EP4220	19980707
W: AL, AU, BR, CA, CN, CZ, HU, ID, IL, JP, KR, MX, NO, NZ, PL, RO, UA, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2265671	A1	19990121	CA 1998-2265671	19980707
AU 9888583	A	19990208	AU 1998-88583	19980707
EP 925289	A1	19990630	EP 1998-940170	19980707
R: DE, ES, FR, GB, IT, SE				
JP 2001500533	T	20010116	JP 1999-508146	19980707
US 6482827	B1	20021119	US 1999-147798	19990310
PRIORITY APPLN. INFO.:			GB 1997-14548	A 19970710
			GB 1997-24395	A 19971118
			WO 1998-EP4220	W 19980707

OTHER SOURCE(S): MARPAT 130:139360
GI



I II



III

AB Title compds. I [W = CONHOH or COOH; R1 and R2 = H or an organic residue; R3 = organic group; Q = secondary or tertiary acyclic or cyclic amido group) and their pharmaceutically acceptable salts, solvates, and hydrates are disclosed as inhibitors of matrix metalloproteinases (MMPs), and of the release of tumor necrosis factor-alpha (TNF) from cells. The compds. are

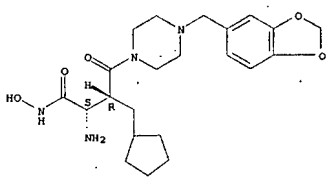
therefore useful in the prevention, control and treatment of diseases in which MMPs or TNF are involved, especially tumoral and inflammatory diseases. Processes for their preparation, and pharmaceutical compns. containing them are also described. For instance, the intermediate 4(S)-(benzyloxycarbonyl)-1-(tert-butoxycarbonyl)-3(R)-isobutylazetidin-2-one (II; preparation given) was subjected to a sequence of ring opening/amidation with piperidine, followed by hydrogenolytic deprotection of the benzyl ester, amidation with PhCH2ONH2.HCl, another hydrogenolysis of the benzyl ether, and acidic deprotection of the BOC-amino group, to give title compound III. The latter compound showed superior aqueous solubility (> 9.5 mg/mL at 25°), and had Ki values as follows: MMP-1 0.088, MMP-2 0.29, and MMP-3 2.5, all in μM.

IT 220046-45-7P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of succinyl piperidinamides, morpholinamides, and piperazinamides as matrix metalloproteinase inhibitors)

RN 220046-45-7 CAPLUS

CN 1-Piperazinebutanamide, α-amino-4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy-γ-oxo-, (αS,βR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

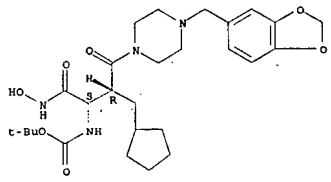


IT 220046-44-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of succinyl piperidinamides, morpholinamides, and piperazinamides as matrix metalloproteinase inhibitors)

RN 220046-44-6 CAPLUS

CN Carbamic acid, [(1S,2R)-3-[4-(1,3-benzodioxol-5-ylmethyl)-1-piperazinyl]-2-(cyclopentylmethyl)-1-[(hydroxyamino)carbonyl]-3-oxopropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

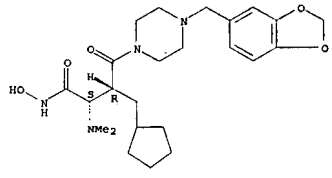


IT 220046-55-9P 220046-57-1P 220046-70-8P
220046-82-2P 220046-88-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of succinyl piperidinamides, morpholinamides, and piperazinamides as matrix metalloproteinase inhibitors)

RN 220046-55-9 CAPLUS

CN 1-Piperazinebutanamide, 4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-α-(dimethylamino)-N-hydroxy-γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

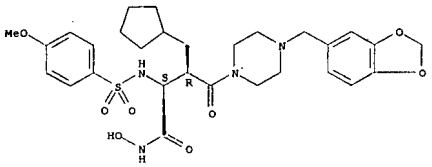
Absolute stereochemistry.



RN 220046-57-1 CAPLUS

CN 1-Piperazinebutanamide, 4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy-α-[[(4-methoxyphenyl)sulfonyl]amino]-γ-oxo-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

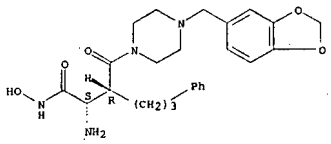


RN 220046-70-8 CAPLUS
CN 1-Piperazinebutanamide, α-amino-4-(1,3-benzodioxol-5-ylmethyl)-N-hydroxy-γ-oxo-β-(3-phenylpropyl)-, (αS,βR)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220046-69-5
CMF C25 H32 N4 O5

Absolute stereochemistry.



CM 2

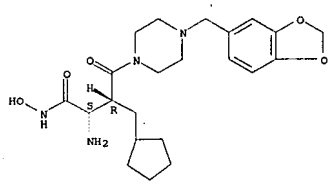
CRN 76-05-1
CMF C2 H F3 O2

RN 220046-82-2 CAPLUS
CN 1-Piperazinebutanamide, α-amino-4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy-γ-oxo-, (αS,βR)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220046-45-7
CMF C22 H32 N4 O5

Absolute stereochemistry.



CM 2

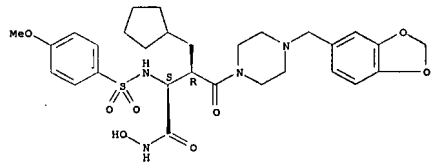
CRN 76-05-1
CMF C2 H F3 O2

RN 220046-88-8 CAPLUS
CN 1-Piperazinebutanamide, 4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy-α-[[(4-methoxyphenyl)sulfonyl]amino]-γ-oxo-, (αS,βR)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220046-57-1
CMF C29 H38 N4 O8 S

Absolute stereochemistry.



CM 2

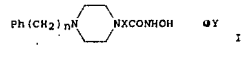
CRN 76-05-1
CMF C2 H F3 O2

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1979:604719 CAPLUS
DOCUMENT NUMBER: 91:204719
TITLE: Pharmaceutical compositions containing piperazinyl acylhydroxamic acid derivatives to treat inflammation or anaphylactic allergy conditions
INVENTOR(S): Coutts, Ronald T.; Biggs, David F.; Wandelmaier, Frank W.; Semaka, Frank D.
PATENT ASSIGNEE(S): Canadian Patents and Development Ltd., Can.
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

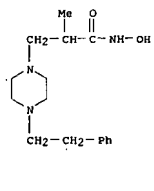
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4166116	A	19790828	US 1977-850825	19771111
CA 1095832	A1	19810217	CA 1978-315010	19781031
PRIORITY APPLN. INFO.:			US 1977-850825 A	19771111

OTHER SOURCE(S): MARPAT 91:204719
GI



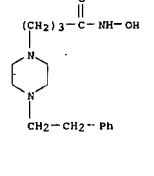
AB Seven piperazinylacylhydroxamic acids I (X = straight or branched C1-3 alkylene, m = 0, 1, or 2, Y = a salt forming acid (when present)] derivs. were prepared by aminoesterification of the corresponding 1-monosubstituted piperazines and then converted to the HCl salts. The compds. showed antiinflammatory, antianaphylactic, and antidepressant activities. Thus, 2-methyl-3-[1-(4-phenyl)piperazinyl]propionohydroxamic acid-HCl [71861-77-3] inhibited carrageenan-induced edema volume by 23.5% 1 h after s.c. administration to rats, decreased egg albumin-induced anaphylaxis by 72% when given i.v. to rats (50 mg/kg), and protected 92% of reserpinized rats given 32 mg of the compound/kg, i.p.
IT 71861-78-4P 71861-81-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antiinflammatory and antianaphylactic activity of)
RN 71861-78-4 CAPLUS
CN 1-Piperazinepropanamide, N-hydroxy-α-methyl-4-(2-phenylethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 71861-81-9 CAPLUS
CN 1-Piperazinebutanamide, N-hydroxy-4-(2-phenylethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl